Remarks

A Request for Continued Examination under 37 C.F.R. § 1.114, including the fee set forth in C.F.R. § 1.17(e), was filed on May 19, 2003 in response to the latest Office Action. In accordance with the Applicants' Request for Continued Examination, the Applicants submit herewith amendments and remarks for the Examiner's consideration.

The Applicants have amended Claim 3 to include that a disulfide bond exists between the two heavy chains of the heterodimer complex. Support for this amendment can be found throughout the Specification, and more specifically page 22, lines 2-3, wherein it is stated that "the heterodimer is linked by the disulfide bond between immunoglobulin heavy chains." Experimental support for the existing disulfide bond is found on page 45 to 49, including Examples 6 and 7 of the Applicants' specification, and page 59-60, Examples 14-15. The Applicants data suggest that the chimeric protein heterodimer complex is a result of a disulfide bond between IgG heavy chain.

Concerning the rejections under 35 U.S.C. § 103, the Examiner is kindly asked to consider the Applicants previous response of April 3, 2003, which based on the latest changes to Claim 3 further distinguishes the functional and structural limitations of the Applicants' heterodimer complex over Carter et al. (U.S. Patent No. 5,821,333)in view of Hori et al (U.S. Patent No. 5,916,771).

Specifically, the protein of the Applicants' claims is a heterodimer complex which comprises a chimeric protein comprising a polypeptide selected from an extracellular portion of a α chain of an integrin and a heavy chain of an immunoglobulin (α chain/IgG heavy chain) and a chimeric protein further comprising a polypeptide selected from an extracellular portion of a β

chain of an integrin and a heavy chain of immunoglobulin (β chain/IgG heavy chain) wherein these chimeric proteins are linked by a disulfide bond. Applicants respectfully submit that as a result of this structure, the Applicants' protein is a soluble heterodimer complex in which an α chain and a β chain are stably associated even under a solubilizing condition, such as culture solutions or a buffer solution. Despite the presence of a solubilizing condition the heterodimer complex retains function in ligand binding form by linking the polypeptide selected from extracellular portions of the α chain and β chain of the integrin with a disulfide bond.

Applicants respectfully submit that Carter et al. merely discloses that a heterodimer complex protein is formed by the introduction of a proturberence at the interface of a first polypeptide resulting in a corresponding cavity in the interface of a second polypeptide to form a hetero-oligomer. Applicants further submit that Hori et al. discloses a heterodimer complex comprising polypeptides linked respectively to an IgG heavy chain and an IgG light chain. Hori et al. only hints that this particular method may apply to the formation of a heterodimer comprising α and β1 integrin and IgG heavy and light chain.

The combination of Carter et al. and Hori et al. only proposes the possibility that a hetero-oligomer may be formed through the binding of a β1 integrin polypeptide to an IgG heavy chain and introduction of a cavity and a protruberence therein. Neither Carter et al. nor Hori et al. disclose either: 1) fusing an extracellular portion of an α chain and a extracellular portion of a β chain of an integrin respectively with an IgG heavy, or 2) linking an extracellular portion of an α chain and a extracellular portion of a β chain of a integrin by a disulfide bond to obtain an integrin heterodimer wherein the α chain and the β chain are stably associated to retain function despite the fact that it has been solubilized.

In view of the foregoing, Applicants respectfully request that the Application is in condition for allowance, which action is respectfully requested.

Respectfully submitted,

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